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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/346,470	07/01/1999	RONALD JOHNSTON HILL	53-99	2471

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	16

DATE MAILED: 02/22/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/346,470	HILL ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 December 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-39* is/are pending in the application.

4a) Of the above claim(s) *8,10,11,19,21,30 and 33-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9,12-18,20,22-29,31 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *13* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IV, claims 1-7, 9, 12-18, 20, 22-29, 31-32 drawn to a nucleic acid encoding a protein with the amino acid sequence of SEQ ID NO: 10, a vector , a host cell, and a method of hybridization in Paper No. 15, 12/10/2001 is acknowledged. The traversal is on the ground(s) that i) there is a shared technical feature. This is not found persuasive because, as set forth in the Restriction requirement, Paper No. 12, 5/8/2001 the nucleic acids and proteins are structurally and functionally distinct, and thus do not have a shared technical feature.

The requirement is still deemed proper and is therefore made FINAL. Claims 8, 10-11, 19, 21, 30, 33-39 are withdrawn from consideration as being drawn to a non-elected invention. Claims 1-7, 9, 12-18, 20, 22-32 are under consideration.

Claim Objections

2. Claims 1-7, 9, 12-18, 20, 22-32 are objected to because of the following informalities: They are drawn to a non-elected invention. Appropriate correction is required.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 1-7, 9, 12-18, 20, 22-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid encoding a polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 10, does not

reasonably provide enablement for an isolated nucleic acid encoding a bioactive derivative or analogue thereof, or a polypeptide which is 40% identical to an amino acid sequence as set forth in SEQ ID NO: 10. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claim 1 is overly broad in the recitation of " bioactive derivative or analogue thereof " or a polypeptide which is 40% identical to SEQ ID NO: 10 since no guidance is provided as to which of the myriad of nucleic acid sequences encoding polypeptide species encompassed by the claim will retain the characteristics of an ecdysone receptor. In the specification (page 40, lines 3-7), Applicants disclose that variants of the polypeptide can be generated by additions substitutions or deletions, such as by site-directed mutagenesis, without disclosing any actual or prophetic examples on expected performance parameters of any of the possible muteins of ecdysone receptor. However, it is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. For example, Mikayama et al. (1993) teaches that the human glycosylation-inhibiting factor (GIF) protein differs from human migration inhibitory factor (MIF) by a single amino acid residue (page 10056, Figure 1). Yet, despite the fact that these proteins are 90% identical at the amino acid level, GIF is unable to carry out the function of MIF, and MIF does not exhibit GIF bioactivity (page 10059, second column, third paragraph). It is also known in the art that a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another

in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph).

There is no guidance provided in the specification as to how one of ordinary skill in the art would generate a nucleic acid sequence encoding an ecdysone receptor other than those exemplified in the specification. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: (1) the breadth of the claims; (2) the nature of the invention; (3) the state of the prior art; (4) the level of one of ordinary skill; (5) the level of predictability in the art; (6) the amount of direction provided by the inventor; (7) the existence of working examples; and (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. Given the breadth of claims 1-7, 9, 12-18, 20, 22-29, 31-32 in light of the predictability of the art as determined by the number of working examples, the level of skill of the artisan, and the guidance provided in the instant specification and the prior art of record, it would require undue experimentation for one of ordinary skill in the art to make and use the claimed invention.

4. Claims 1-7, 9, 12-18, 20, 22-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. In the specification (page 40, lines 3-7), Applicants disclose that variants of the polypeptide can be generated by additions substitutions or deletions, such as by site-directed mutagenesis, to SEQ ID NO: 10. The specification and claims do not indicate what distinguishing attributes the members of the genus share. Thus, the scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Although the specification states that these types of changes are routinely done in the art, the specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. Insufficient common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a nucleic acid encoding SEQ ID NO: 10 alone is insufficient to describe the genus. One of skill in the art would reasonably conclude that the disclosure fails to provide a

representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

5. Claims 1-7, 9, 12-18, 20, 22-29, 31-32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The deposit of the biological material is considered necessary for the enablement of the current invention (see MPEP Chapter 2400 and 37 C.F.R. §§ 1.801-1.809). Elements required for practicing a claimed invention must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. The specification is not fully compliant with all of the provisions for maintenance and availability of the deposited material. If a deposit is made under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure (e.g. see 961 OG 21, 1977), and Applicants, their assignee or their agent needs to provide a declaration containing the following: i) a statement all restrictions on the availability to the public of the deposited material so deposited will be irrevocably removed upon the granting of a patent. ii) A statement that the material has been deposited under conditions that assure that access to the material will be available during the pendancy of the patent application to one determined by the Commissioner to be entitled thereto under 37 C.F.R. 1.14 and 35 U.S.C. § 122. iii) A statement that the deposited material will be maintained with all of the care necessary to keep it viable and uncontaminated for a period of at least five years after the most recent request for the furnishing of a sample of the deposited microorganism, and in any case, for a period of at least thirty years

after the date of deposit or for the enforceable life of the patent, whichever period is longer. iv) A statement by declarant that all statements are true and that all statements made on information and belief are believed to be true; and further that these statements were made on information and belief are believed to be true; and further that these statements were made with knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under 18 USC § 1001 and that such willful false statements may jeopardize the validity of the instant patent application or any patent issuing thereon.

Claim Rejections - 35 USC § 112 second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-7, 9, 12-18, 20, 22-29, 31-32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 4, 8, 10, 11, 12, 13, 14, 15 are vague and indefinite in the recitation of the terms "EcR" and "USP". There is no definition within the claim to define the protein to which these acronyms refer. Thus, the metes and bounds of this claim cannot be determined. Claims 2-3, 5-7, 9, 16 are rejected insofar as they depend on the recitation of the terms "EcR" and "USP".

Claim 6 recites the term "close-relative", which is a conditional term and renders the claim indefinite. The metes and bounds of the claim thus cannot be ascertained. This rejection could be obviated by supplying specific parameters supported by the specification which Applicant considers to be a "close-relative" of an *M. persicae* insect.

Claims 1, 7, 12, 17, 22, 25, are indefinite in the recitation of the term "bioactive analogue". There is insufficient guidance as to what the bioactivity is, thus the metes and bounds of the claims cannot be determined. Claims 2-6, 13-16, 18, 23-24, 26-29, 31-32 are rejected insofar as they depend on the recitation of the term "bioactive analogue".

The term " hybridization-effective amount " in claims 22, 25 is a relative term which renders the claim indefinite. The term " hybridization-effective amount " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention. Claims 23, 26-26-27 are rejected insofar as they depend on the recitation of the term " hybridization-effective amount ".

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-7, 9, 12-18, 20, 22-29, 31-32 are rejected under 35 U.S.C. 102(a) as being anticipated by Mouillet et al. (1997).

Mouillet teaches the cloning and isolation of two nucleic acids encoding homologs of the *T. molitor* ecdysteroid receptor (page 857, column 1, first paragraph). The polypeptide encoded by the nucleic acid taught by Mouillet is at least 40% identical to the amino acid sequence of the polypeptide set forth in the instant case as SEQ ID NO: 10 (see Sequence Comparison A,

attached), thus claim 1 is anticipated. The nucleic acid taught by Mouillet is an insect ecdysteroid receptor, thus anticipating claims 2-6, 9. Due to the indefinite nature of the limitation 'bioactive analogue", claims 7, 12-18 are anticipated.

Mouillet teaches a method of hybridization using the disclosed nucleic acid molecules which encode steroid receptor polypeptides (page 860, Figure 4). The nucleic acid encoding the Ecdysone receptor polypeptide has regions of identity to SEQ ID NO: 9 that are at least 10 nucleotides long, thus claims 22-27 are anticipated. Mouillet teaches the construction of vectors comprising their disclosed nucleic acid, as well as host cells on page 857, column 2, second paragraph), thus claims 28-29 and 31-33 are anticipated.

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
February 19, 2002

DAVID S. ROMEO
PRIMARY EXAMINER